Citation:

Griel AE, Cao Y, Bagshaw DD, Cifelli AM, Holub B, Kris-Etherton PM. A macadamia nut-rich diet reduces total and LDL-cholesterol in mildly hypercholesterolemic men and women. *J Nutr.* 2008 Apr; 138 (4): 761-767.

PubMed ID: 18356332

Study Design:

Randomized crossover trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To evaluate the lipid and lipoprotein responses of a blood cholesterol-lowering diet that contained macadamia nuts, using the serving size defined in the qualified health claim for tree nuts and peanuts (1.5 oz per 2,100kcal) vs. the average American diet.

Inclusion Criteria:

- Non-smoker
- BMI 22-35kg/m^2
- LDL-C: 25-90th percentile NHANES (2.64-4.53mmol/L)
- HDL-C: 25-90th percentile NHANES (0.88-1.79mmol/L)
- Not on lipid-lowering medication or other medications known to affect lipid levels.

Exclusion Criteria:

Subjects who reported an allergy to nuts or an aversion to consuming nuts.

Description of Study Protocol:

Recruitment

Recruited via advertisements in the local newspaper and fliers distributed across the campus of the Pennsylvania State University.

Design

Randomized, two-period crossover design.

Blinding Used

Subject's chemistry and lipid panels were screened by different personnel than Metabolic Diet Study Center personnel who provided experimental and control meals.

Intervention

- A five-week macadamia nut-rich (MAC) diet of 1.5oz per 2,100kcal at 33% total fat (7% saturated fatty acids,18% monounsaturated fatty acids and 5% polyunsaturated fatty acids) was administered for one period
- The other period intervention was the average American diet (AAD), a diet patterned after the typical American intake
- The two diets were matched for total fat, protein and carbohydrate
- There was a two-week compliance break between each diet period, during which subjects consumed their usual diets.

Statistical Analysis

- Boxplot and interquartile range generated for variables at baseline to determine outliers which were then not included in impact analysis. Final analysis represent the removal of the following number of data points for each of the lipid and lipoproteins: Total cholesterol (six), LDL-C (five), HDL-C (three) and triglycerides (three) including CVs that ranged from 12 to 49%
- Shapiro-Wilk test of the residuals from the mixed model was used to test for the normality of each variable. A W statistic >0.90 indicated that the variable was normally distributed. All analyses were performed on transformed values; all means reported represent unadjusted means
- Mixed models procedure (PROC MIXED) was used to test for effects of diet, gender, order of diet presentation, period and their interactions on the levels of all outcome variables. Tukey-Kramer adjusted P-values<0.05 were used to determine whether the differences in the outcome variables were significant
- Pearson correlations were performed both across all diets and within each diet to investigate possible relationships between the calculated ratios of fatty acids (18:1/18:0 and 16:1/16.0) and each of the outcome variables (i.e., Total cholesterol, LDL-C, HDL-C, and triglycerides)
- Stepwise regression analysis was used to examine the relationship between calculated fatty acid ratios and serum TG concentrations. An increase in R^2 ($P<0.05$ with the addition of a variable was considered significant in the regression equation.

Data Collection Summary:

Timing of Measurements

Dependent variables were measured at baseline and at the end of each of the two five-week diet periods.

Dependent Variables

- Serum fatty acids were quantified according to a standard protocol and serum concentrations of oleic (18:1), stearic (18:0), palmitoleic (16:1) and palmitic (16:0) acids were used to calculate two different desaturation indices (18:1/18:0 and 16:1/16:0) as an in vivo measure of stearoyl-CoA desaturase (SCD) activity
- Serum lipids and lipoproteins were measured. Serum total cholesterol (TC) and TG concentrations were quantified using enzymatic assays. HDL-C was estimated according to

the modified heparin-manganese precipitate procedure of Warnick and Albers. LDL-C concentrations were calculated by the Friedewald equation: LDL-C=TC -(HDL-C+TG/5).

Independent Variables

- Macadamia nut-rich diet (MAC) included 1.5oz per day of macadamia nuts per 2,100kcal
- Average American diet (AAD) was patterned after the typical American intake as detained in the Continuing Survey of Food Intakes by Individuals and NHANES database and the two diets were matched for total fat, protein and carbohydrate.

Control Variables

Subjects were instructed to maintain their usual activities and exercise levels throughout the study.

Description of Actual Data Sample:

- *Initial N:* 25 subjects were recruited (10 men and 15 women)
- *Attrition (final N):* 24 (However, screening and diet period one data for this subject was included in the analysis)
- *Age:* 50.2±8.4 years
- *Ethnicity:* Not specified in report
- *Other relevant demographics:*
  - The study population represented a mildly hypercholesterolemic group with a TC concentration of 5.40±0.69mmol/L and LDL-C concentration of 3.46±0.55mmol/L
- *Anthropometrics:* None
- *Location:* Pennsylvania State University Campus, US.

Summary of Results:

Key Findings

- Serum saturated fatty acids were lower and monounsaturated fatty acids were higher following consumption of the macadamia nut-rich diet (MAC) compared with the average American diet (AAD)($P<0.05$). Serum polyunsaturated fatty acids concentration did not change
- The calculated serum fatty acid ratio of 18:1/18:00 (oleic/stearic) was higher following the MAC diet compared with baseline ($P<0.001$)
- The serum fatty acid ratio of 16:1/16:0 (palmitoleic/palmitic) was greater following the MAC diet compared with both baseline and the AAD control diet ($P\leq0.0001$)
- The consumption of the MAC diet resulted in lower serum total cholesterol (TC), LDL-C, and non-HDL-C concentrations compared with baseline and to after the AAD control diet period ($P<0.0001$). Compared with the AAD control diet the MAC diet elicited a 9.4% reduction in TC concentration and a 8.9% reduction in LDL-C concentration
- The ratios of TC: HDL-C and LDL-C: HDL-C were both lower following the consumption of the MAC diet than the AAD and baseline
- The calculated stearoyl-CoA desaturase (SCD) ratios were correlated with concentrations of serum triglycerides ($r=0.48$; $P\leq0.0001$) and HDL-C ($r= -0.42$; $P<0.0001$) across all diets, however, the SCD ratio was not correlated with serum TC or LDL-C concentration
- Regression analysis revealed a stronger predictive value for both calculated SCD ratios

following consumption of the AAD diet (16:1/16:0, R^2=0.40; P<0.01 and 18:1/18:0, R^2=0.37; P<0.01) compared with the MAC diet (16:1/16:0. R^2=0.16; P<0.05 and 18:1/18:0, R^2=0.16; P<0.05. The ratio of serum 16:1/16:0 predicted 29% of the variance in TG at baseline (P<0.01); 18:1/18:0 was not a significant predictor of serum TG concentrations at baseline.

Serum Lipids and Lipoproteins in Subjects at Baseline and After Consuming AAD and MAC Diets for Five Weeks Each[1]

Variable[2]	Baseline	AAD	MAC
TC, mmol/L	5.66±0.17	5.45±0.17[b]	4.94±0.17[a,b]
LDL-C, mmol/L	3.68±0.14	3.44±0.14[b]	3.14±0.14[a,b]
HDL-C, mmol/L	1.24±0.05	1.20±0.05[b]	1.11±0.05[a,b]
Non-HDL-C, mmol/L	4.41±0.17	4.26±0.17	3.83±0.17[a,b]
TC: HDL-C	4.79±0.24	4.89±0.24	4.60±0.24[a]
LDL-C: HDL-C	3.15±0.17	3.09±0.18	2.91±0.17[a,b]

[1]Values are least-square means ±SD, N=25

[a]Different from AAD, P<0.05

[b]Different from baseline, P<0.005 (post hoc Tukey comparisons from multi-factor ANOVA)

[2]Conversion factors: Cholesterol, 1mg/dL=0.0259mmol/L; TG, 1mg/dL=0.0113mmol/L.

Author Conclusion:

The author reports this study demonstrates that inclusion of 1.5 ounces of macadamia nuts in a cholesterol-lowering diet significantly reduces total cholesterol and LDL-C concentrations.

Reviewer Comments:

- *Relatively small sample size; unclear whether 1.5 ounces of macadamia nuts consumed for five weeks led to results*
- *The author stated the SCD ratio was more likely affected by intake of MUFA than changes in SCD activity and that direct measures of SCD may be necessary to make meaningful conclusions about 18:1 and 16:1 activity.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes

2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	???
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	No
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A

3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	No
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes

6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	???
9.1.	Is there a discussion of findings?	Yes

9.2.	Are biases and study limitations identified and discussed?	No
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes